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Long term impact of the low FODMAP diet on gastrointestinal symptoms, dietary intake, patient acceptability and healthcare utilisation in irritable bowel syndrome

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Running title: Long-term impact of the low FODMAP diet

Abbreviations:

DRV, dietary reference value; FODMAP(s), fermentable oligosaccharides, disaccharides, monosaccharides and polyols; IBS, irritable bowel syndrome; NICE, National Institute for Health and Care Excellence; QOL, quality of life; RCT, randomised controlled trial; SD, standard deviation

Keywords:

FODMAP; nutrient intake, diet, irritable bowel syndrome

Abstract

Background

The low FODMAP diet is a frequently used treatment for irritable bowel syndrome (IBS). Most research has focused on short-term FODMAP restriction however guidelines recommend that high FODMAP foods are reintroduced to individual tolerance. This study aimed to assess the long-term effectiveness of the low FODMAP diet following FODMAP reintroduction in IBS patients.

Methods

Patients with IBS were prospectively recruited to a questionnaire study following completion of dietitian-led low FODMAP education. At baseline and following FODMAP restriction (short-term) only gastrointestinal symptoms were measured as part of routine clinical care. Following FODMAP reintroduction, (long-term), symptoms, dietary intake, acceptability, food-related quality of life (QOL) and healthcare utilisation were assessed. Data were reported for patients who continued long-term FODMAP restriction (adapted FODMAP) and/or returned to a habitual diet (habitual).

Key Results

Of 103 patients, satisfactory relief of symptoms was reported in 12% at baseline, 61% at short-term follow-up and 57% at long-term follow-up. At long-term follow-up, 84 (82%) patients continued an 'adapted FODMAP' diet (total FODMAP intake mean 20.6, SD 14.9g/d) compared with 19 (18%) of patients following a 'habitual' diet (29.4, SD 22.9g/d, $p=0.039$). Nutritional adequacy was not compromised for either group. The 'adapted FODMAP' group reported the diet cost significantly more than the 'habitual' group ($p<0.001$) and affected social eating ($p<0.01$) but there was no effect on food-related QOL. Healthcare utilisation was similar between both groups.

Conclusion and Inferences

Low FODMAP education is effective for long-term IBS management, enables a nutritionally adequate diet and is broadly acceptable to patients.

Key Points

The low FODMAP diet is a successful treatment for irritable bowel syndrome (IBS). However, there are limited data on the long-term effects of the diet. The current study assessed the long-term impact of the low FODMAP diet on clinical response, dietary intake, patient acceptability, food-related QOL and healthcare use.

Over half of patients report long-term symptom relief, the diet is nutritionally adequate and acceptable to patients.

The findings support using the low FODMAP diet for long-term IBS management.

Introduction

Irritable bowel syndrome (IBS) is the most commonly diagnosed gastrointestinal disorder[1] and is characterised by episodic abdominal pain and altered defecation[2]. This heterogeneous disorder is a leading cause of morbidity among the general population and global prevalence is estimated at 11% with women more commonly affected than men[3]. It has a significant impact on patients' health-related quality of life (QOL)[4, 5] and is associated with increased healthcare utilisation [6] and has significant economic consequences[1, 7]. Over 80% of IBS patients report food-related symptoms and this is independently associated with reduced QOL[8].

Dietary restriction of fermentable oligosaccharide, disaccharide, monosaccharide and polyols (low FODMAP diet) is an effective treatment for IBS symptoms, with 50-76% of patients demonstrating a clinical response[9-15]. Randomized[10, 13, 16, 17] and non-randomized trials[14, 15, 18] demonstrate short-term (up to 6 weeks) global and individual symptom improvement in IBS and have been reviewed elsewhere[19]. The diet involves restriction of high FODMAP foods for 4-6 weeks to achieve symptom improvement followed by systematic reintroduction to identify the tolerance threshold for individual FODMAPs, which enables long-term self-management of symptoms and increasing dietary variety.

The low FODMAP diet is a complex intervention and should be implemented with counselling from a dietitian[20-22]. To date, research has reported on clinical and nutritional outcomes following short-term FODMAP restriction[10, 13]. However, there are concerns regarding the nutritional adequacy of the diet and inadequate calcium intake following four weeks of FODMAP restriction[13]. Furthermore, there are concerns regarding long-term acceptability of the diet[12, 18]. Data on the long-term effectiveness, nutritional adequacy and acceptability of the low FODMAP diet are scarce. For example, studies have reported symptoms retrospectively[12, 23] or symptoms and acceptability prospectively[18, 24]. However, there has been no evaluation of dietary intake or other aspects of the diet in relation to food-related QOL and effects on healthcare utilization in the long term.

The extensive elimination of foods and the likelihood that many patients that respond will require dietary modification in the long term, coupled with the increasing use of the low FODMAP diet warrants a comprehensive evaluation of long-term outcomes. Therefore, the aims of this study were to assess the long-term impact of the low FODMAP diet on clinical response, high and low FODMAP food frequency, nutritional adequacy, dietary acceptability, food-related QOL and healthcare utilization in patients with IBS.

Materials and Methods

Study design

This study was a prospective long-term follow-up postal questionnaire study. Consecutive patients diagnosed with IBS in accordance with the National Institute of Health and Care Excellence (NICE) (abdominal pain/discomfort, bloating or change in bowel habit for at least 6 months in the absence of organic disease)[21] were recruited from both secondary care (Guy's and St Thomas' NHS Foundation Trust, London, UK) and primary care (Somerset Partnership NHS Foundation Trust, Somerset, UK). All eligible patients had been counselled on the low FODMAP diet by a specialist gastroenterology dietitian and had received two clinical appointments; the initial appointment for dietary education on FODMAP restriction (baseline) and the follow-up appointment at least 6 weeks later when they had been following the low FODMAP diet (short-term follow-up) at which point they were educated on FODMAP reintroduction. The prospective long-term follow-up performed as part of this study (long-term follow-up) occurred at least 6 months and no more than 18 months after short-term follow-up. Thus, data were collected from three time points, the first two of which were part of routine clinical care where only symptom data were collected.

At baseline, patients had been instructed to restrict their intake of high FODMAP foods for at least 6 weeks. Written guidance on suitable and unsuitable foods and appropriate low FODMAP food products for the restriction phase of the diet was provided. At short-term follow-up, counselling on FODMAP reintroduction was provided. Patients were instructed to undertake 3-day FODMAP food

challenges using increasing food portions to identify individual FODMAPs that triggered symptoms. This process enabled patients to reintroduce some high FODMAP foods to their tolerance threshold. Both appointments were conducted as per normal clinical practice as described elsewhere[14, 15].

Patients were ineligible for the prospective long-term follow-up study if they had failed to attend the short-term follow-up clinical appointment; had experienced an acute gastrointestinal episode in the four weeks prior to long-term follow-up; had been diagnosed with a co-existing gastrointestinal disease (e.g. inflammatory bowel disease, coeliac disease), an eating disorder or a significant psychiatric disorder since baseline; or were unable to give informed consent.

The study was carried out in accordance with the Declaration of Helsinki and was approved by the East of Scotland Research and Ethics Committee (REC reference: 13/ES/0158). Participation was voluntary and all data were confidential and were reported anonymously. All patients provided written informed consent at long-term follow-up.

At the prospective long-term follow-up patients were asked to report their current weight and height and whether their weight had changed during FODMAP restriction. Patients were also asked to rate their current knowledge of the low FODMAP diet using a 5-point Likert scale (extremely poor; below average; average; above average; excellent).

Gastrointestinal symptoms and stool output

Data for symptoms and stool output were available for baseline, short-term follow-up (from clinical records) and long-term follow-up (from prospective survey). Data from baseline and short-term follow-up clinical appointments were matched to the long-term follow-up data using a unique anonymised identifier.

Global symptom response used the question "*Do you currently have satisfactory relief of your gut symptoms?*"[25]. The Gastrointestinal Symptom Rating Scale (GSRS) was used to assess the severity (absent, mild, moderate, severe) of abdominal pain, bloating, flatulence, burping, borborygmi,

urgency, incomplete evacuation, nausea, heartburn, acid regurgitation and lethargy[26]. Data on stool frequency and consistency (Bristol stool form scale) were collected at all time points and based on an average for the last 7 days[27]. IBS subtype was based on retrospective reporting of predominant stool consistency: those reporting Bristol Stool Form type 1 or 2 were classified as constipation-predominant IBS (IBS-C), those reporting Bristol Stool Form type 6 or 7 were classified as diarrhoea-predominant IBS (IBS-D), those reporting Bristol Stool Form type 1 or 2 and 6 or 7 were classified as mixed subtype IBS (IBS-M) and those reporting Bristol Stool Form type 3, 4 or 5 were classified as IBS unclassified (IBS-U).

Dietary intake, acceptability and food-related quality of life

Dietary intake was assessed at long-term follow-up using the Comprehensive Nutrition Assessment Questionnaire (CNAQ) which is a semi-quantitative food frequency questionnaire validated to assess FODMAP and nutrient intake[28]. FODMAP intake was determined using an automated entry system available online (http://www.cnaq.com.au). Nutritional adequacy was assessed by comparison of nutrient intakes against the United Kingdom dietary reference values[29-31]. Frequency data on the consumption of foods high and low in individual FODMAPs was assessed based on cut-offs[32]. Each food frequency questionnaire food item was categorised as high or low FODMAP and, if high, which FODMAP(s) they contained. Food items were also categorised into food groups and subgroups to assess daily intakes. Low FODMAP speciality foods were included within their respective food group, e.g. low FODMAP cereals and grains included gluten-free bread, and low FODMAP milk included lactose-free cow's milk. Additionally, daily intakes of onion and garlic were assessed as they contribute a large amount of fructans to the diet[33].

The proportion of patients who consumed foods high in individual FODMAPs (fructans, galacto-oligosaccharides, lactose, fructose, sorbitol and mannitol) at least once a week was assessed between groups.

Patients were asked to record their dietary adherence to long-term FODMAP restriction using a 4-point Likert scale: 'continued strict low FODMAP diet', 'reintroduced high FODMAP foods to tolerance', 'continued low FODMAP diet 50% of the time', 'returned to habitual diet'. The 'adapted FODMAP' group included the first three of these.

Acceptability of dietary restriction was assessed at long-term follow-up using a 14-item questionnaire adapted from the nutrition-related QOL questionnaire[34]. Questions considered the impact and challenges of diet on eating environment, travel, meal enjoyment, cost, shopping and cooking. Data were scored using a 5-point Likert scale (strongly agree, agree, neutral, disagree, strongly disagree).

The impact of the low FODMAP diet on QOL was assessed at long-term follow-up using a 7-item questionnaire based on a generic validated food-related QOL tool (Satisfaction with Food-related Life)[35]. Data were scored using a 5-point Likert scale (strongly agree, agree, neutral, disagree, strongly disagree).

Healthcare utilisation and work absenteeism

At long-term follow-up patients were asked to record how often they visited their general practitioner or gastroenterologist for gastrointestinal symptoms during the previous 12 months, what IBS medication they were currently taking, if it had changed since being advised on the low FODMAP diet and whether they were absent from work due to their gastrointestinal symptoms in the same period.

Statistical analysis

The primary outcome was global symptom relief at long-term follow-up compared with baseline. The sample size was calculated to detect a difference in the primary outcome assuming 60% of patients who had reported global symptom relief at short-term follow-up would continue to report it at long-term follow-up versus 10% of patients who had not reported global symptom relief at short-

term follow-up would report it at long-term follow-up. A total of 80 completed questionnaires were required at 90% power for detecting a difference in the primary outcome at p=0.05 significance level. From previous experience of postal invitation to a dietary intake study, it was anticipated that at least 20% of subjects invited would complete and return the questionnaires[36], thus it was assumed that 380 patients would be invited to achieve the sample size requirement.

Returned questionnaires were excluded from analysis if more than 10% of questions had not been answered. Individual symptom responses assessed by the GSRS were collapsed into a dichotomous response to report the presence or absence of 'moderate or severe' symptoms as previously reported[15]. Stool frequency was reclassified into normal (once every 3 days to three times a day) or abnormal (less than once every 3 days or more than three times a day). Stool consistency was reclassified into normal (Bristol Stool Form types 3, 4 or 5) or abnormal (Bristol Stool Form types 1, 2, 6 or 7) as previously reported[15]. For dietary intake, dietary acceptability, food-related QOL, work absenteeism and healthcare utilisation comparisons, patients were collapsed into a dichotomous response set according to whether they returned to a habitual diet ('habitual') or continued to restrict high FODMAP foods ('adapted FODMAP') at long-term follow-up. Categorical data for dietary acceptability and food-related QOL were collapsed into three group response sets to provide clinically meaningful interpretation and data distribution for analysis.

All data were analysed using SPSS, version 22 (SPSS Inc, Chicago, IL, USA). Demographic and baseline symptoms were analysed descriptively. Data are reported as mean ± standard deviation (SD) with 95% confidence intervals for continuous data and n (%) for categorical data, unless otherwise indicated. A Bonferroni correction was applied for multiple comparisons where required. Statistical significance was considered where $p<0.05$.

Macronutrient and micronutrient intakes were assessed for adequacy in comparison to the UK recommendations. Food frequency intakes from the food frequency questionnaire were converted

to daily intakes using previously published conversion factors[37]. Daily intakes were adjusted to account for the total number of foods reported as consumed by each subject.

Results

A total of 375 (n=309 secondary care, n=66 primary care) patients were eligible and invited to participate in the study. Of these, 232 did not respond to the invitation to participate, thus 143 were consented and recruited (Figure 1). Thirty patients agreed to take part initially but did not return the questionnaire while seven withdrew stating lack of time or personal reasons, and three patients returned incomplete questionnaire and were excluded from analysis. Therefore, 103 patients were analysed at long-term follow-up (Table 1) with 74 from secondary care and 29 from primary care. All baseline demographics were similar between groups except for gender and age. There were significantly fewer males from primary care (females from secondary care 50 (49%), females from primary care 26 (25%), males from secondary care 24 (23%), males from primary care 3 (3%); p=0.022) and the patients recruited from secondary care were significantly younger than the patients recruited from primary care (secondary care 45.3±15 years *vs* primary care 56.6±12 years; p<0.001). At baseline 20 patients had IBS-C, 39 patients had IBS-D, 21 patients had IBS-M and 23 patients had IBS-U.

Gastrointestinal symptoms and stool output

At baseline, 12 (12%) patients reported satisfactory symptom relief, which increased to 63 (61%) patients at short-term follow-up (FODMAP restriction) and to 59 (57%) patients at long-term follow-up (Figure 2; p=0.003). There were no significant differences for satisfactory relief between settings at baseline (secondary care 8 (8%) *vs* primary care 4 (4%); p=0.671), short-term follow-up relief (secondary care 42 (41) *vs* primary care 21 (20%); p=0.143) and long-term follow-up relief (secondary care 41 (40%) *vs* primary care 18 (18%); p=0.539). Of the 63 patients with satisfactory relief at short-term follow-up, 44 (70%) maintained this in the long term. The proportion of patients reporting presence of individual symptoms significantly decreased over time (Figure 3). Specifically,

abdominal pain, bloating and flatulence were reported in over 60% of patients at baseline and decreased by at least a third at long-term follow-up. There was a significant reduction in the proportion of patients reporting abnormal stool frequency (baseline 21%; short-term follow-up 7%; long-term follow-up 7% p<0.001) and abnormal stool consistency (baseline 65%; short-term follow-up 43%; long-term follow-up 42% p=0.001) (Cochran test).

Dietary intake, acceptability and food-related quality of life

At long-term follow-up, 84 (82%) patients continued to follow an 'adapted FODMAP' diet while 19 (18%) returned to a 'habitual' diet. There were no significant differences between groups at long-term follow-up for energy and nutrient intakes, except for folate and vitamin A which were both higher in the 'adapted FODMAP' group compared with the 'habitual' group (Table 2). At least 95% of patients met the appropriate dietary reference value for energy and the majority of nutrients in both groups. Total carbohydrate and calcium intakes, which have previously been reported as lower than controls in short-term low FODMAP diet studies[9, 13], were not different between the 'adapted FODMAP' group compared with the 'habitual' group (total carbohydrate: 250±94.4g/d *vs* 252±95.5g/d, p=0.925; calcium: 960±608mg/d *vs* 1168±695mg/d, p=0.230, respectively).

Total FODMAP intake was significantly lower for the 'adapted FODMAP' group (20.6±14.9g/d) compared with the 'habitual' group (29.4±22.9g/d, p=0.039; Table 2). No significant differences were noted between the groups for individual FODMAP intakes although there was a trend for lower lactose intake in the 'adapted FODMAP' group compared with the 'habitual' group (10.4±12.7g/d *vs* 16.9±19.4g/d, p=0.072).

Patients in the 'adapted FODMAP' group reported a significantly lower overall intake of high FODMAP food groups (1195±658g/d *vs* 1751±1015g/d, p=0.004) and a significantly higher overall intake of low FODMAP food groups (2770±1236g/d *vs* 1857±983g/d, p=0.003) than patients in the 'habitual' group (Table 3). There were similar overall intakes between groups for high and low FODMAP cereals and grains and the only significant findings for sub-groups of cereals and grains sub-

group were that the 'adapted FODMAP' group had a higher intake of low FODMAP bread (difference 27.04g/d, p=0.022) and a lower intake of high FODMAP pasta (difference -26.7g/d, p=0.010) compared with the 'habitual' group. The 'adapted FODMAP' group reported a higher intake of low FODMAP milk and milk products (difference 415g/d, p=0.023), specifically low FODMAP milk (difference 393g/d, p=0.024), and low FODMAP vegetables (difference 220g/d, p=0.020) and a lower intake of fats and oils (difference -11.4g/d, p=0.003) compared with the 'habitual' group.

Patients in the 'adapted FODMAP' group consumed significantly less onion and garlic than patients in the 'habitual' group (onion: (11.4±19.1g/d *vs* 22.9±27.2g/d, p-0.032; garlic 0.32±0.63g/d *vs* 1.25±1.83g/d, p<0.001).

Significantly fewer patients in the 'adapted FODMAP' group ate high fructan foods at least once a week (21% *vs* 30% p<0.001) or foods containing high levels of free-fructose at least once a week (17% *vs* 27% p<0.001) compared with the 'habitual' group, and there were no differences between groups for foods containing high levels of lactose, galacto-oligosaccharides, sorbitol or mannitol (Table 4).

There were no significant differences between groups for the majority of components of dietary acceptability (Table 5) except for the following. Seventy-two (86%) patients in the 'adapted FODMAP' group reported their diet was more expensive than prior to following the diet, compared with only 8 (42%) patients in the 'habitual' group (p<0.001). The 'adapted FODMAP' group reported increased difficulty eating out at restaurants compared with the 'habitual' group (66 (79%) *vs* 11 (58%) p=0.013), eating at family and friends' houses (61 (72%) *vs* 9 (48%) p=0.009) and eating when travelling (63 (76%) *vs* 9 (48%) p=0.014). However, there were no significant differences for any of the components of food-related QOL between groups (Table 5).

Healthcare utilisation and resources

There were no significant differences for healthcare utilisation between the 'adapted FODMAP' and 'habitual' groups for either visiting a GP (33 (39%) *vs* 9 (47%) p=0.431) or gastroenterologist (34 (41%) *vs* 8 (42%) p=0.390). Additionally, there were no significant differences for the numbers of days absent from work between groups with 15 (18%) 'adapted FODMAP' patients *vs* 3 (16%) 'habitual' diet patients (p=0.775) taking at least 3 days off work in the last 12 months due to gastrointestinal symptoms.

Approximately half of patients reported taking no medication at long-term follow-up, 39 (46%) of the 'adapted FODMAP' *vs* 10 (53%) of the 'habitual' group (p=0.625). Since low FODMAP advice, significantly more patients in the 'adapted FODMAP' group, 22 (26%) ceased medication compared with only 1 (5%) patient in the 'habitual' group (p=0.048). For the 'adapted FODMAP' group, 11 (13%) patients started new medication compared with 3 (16%) in the 'habitual' group (p=0.757) and 3 (4%) of the 'adapted FODMAP' group reported a change in medication over the past 12 months compared with no patients in the 'habitual' group (p=0.403).

Patients in the 'adapted FODMAP' group had a greater dependency on supplementary resources to support their diet than those in the 'habitual' group (p<0.001), with just under half of 'adapted FODMAP' patients (42%) using dietary information provided by the dietitian, 19% using websites with low FODMAP recipes and 18% using low FODMAP cookbooks.

Discussion

This is the first study to comprehensively report on the long-term implications of the low FODMAP diet in patients with IBS 6-18 months following dietitian-led education. A majority of patients (82%) educated on the low FODMAP diet continued with a personalised adaptation of the diet to self-manage their symptoms in the long term and 57% of all patients who received low FODMAP education continued to report long-term satisfactory relief. Nutritional requirements were met by the majority of patients and long-term nutritional adequacy was not compromised when compared

with the 'habitual' diet group. Overall, patients found the 'adapted FODMAP' diet acceptable and it did not negatively affect their food-related QOL, healthcare utilization and work absenteeism more than patients who had returned to a 'habitual' diet.

Our finding that dietary adherence to the low FODMAP diet is maintained in the long term and is associated with improved symptom response is indicative of the therapeutic value of the diet for long-term management. Short-term studies have demonstrated consistent and reproducible findings on overall symptoms[10, 13, 14, 16, 17] and emerging, long-term data is also supportive. After a median of 16 months following FODMAP education, 86% of patients with IBS and inflammatory bowel disease reported a partial (54%) or full (32%) symptom response to the diet[23], consistent with our findings. An earlier retrospective study, which investigated adherence and clinical effectiveness of a partial low FODMAP diet (fructose and fructan restriction) found that at 14 months follow-up 77% of patients were adherent to the diet with 76% reporting significant improvement in abdominal symptoms[12]. Prospective data on adherence are similar to our current study; 76% of participants were adherent to the low FODMAP diet at a mean 16 month follow-up, but satisfaction with symptom response was slightly greater at 72% of patients than that observed herein[18]. In a randomised non-blinded trial which compared the low FODMAP diet with hypnotherapy, 82% of patients who had responded to the diet maintained satisfactory relief of symptoms at 6 months, equating to 58% of all patients who had received dietary advice[24]. Cumulatively, long-term adherence to the low FODMAP diet is not only maintained in the majority of patients but is associated with significant improvement in symptom response. The variation observed between studies may be explained, at least in part, by differences in study design such as the high level of response bias in retrospective studies.

Individual symptom severity reduced at both short- and long-term follow-up. Significant reductions in abdominal pain, bloating, flatulence, incomplete evacuation and lethargy were reported, with pain, bloating and flatulence decreasing by more than one third in the long term. These findings are

consistent with existing short[10, 13, 14, 16, 17] and long-term literature [18, 23, 24, 38] as well as a recent systemic review and meta-analysis[39]. The study cohort had a low reporting of abnormal stool frequency at baseline which is not uncommon in IBS due to its relapsing and remitting nature. The enduring symptom alleviation associated with the diet is a remarkable advantage of FODMAP therapy particularly compared to pharmaceutical management where symptom relief is limited at best[40]. Dietary management of IBS is associated with increased feelings of self-control and empowerment[41] and may foster greater long-term self-management.

The lack of robust long-term nutrient data and the identification of at risk nutrients in short-term studies[14] have raised questions regarding the nutritional adequacy, and therefore suitability, of the diet for long-term management. A key finding herein is that an 'adapted FODMAP' diet maintained for 6-18 months achieved nutritional adequacy and any deficits in energy or nutrient intakes were similar to those expected in the background population[42].

In short-term studies of the low FODMAP diet, total carbohydrate intakes of 200 g/d have been observed following FODMAP restriction[9, 13] however the current study reports a 20% higher total carbohydrate intake. A gluten-free diet for management of coeliac disease is associated with a similar trend, that is a reduction in carbohydrate intake observed in patients new to the diet followed by an increase in experienced users[43, 44]. There was no reduction in long-term dietary fibre intake. Data on dietary fibre intakes in short-term studies are inconsistent. Two studies report similar levels to baseline[13, 45] while another shows a significant reduction in intake following FODMAP restriction[9]. A reduction in dietary fibre intake during FODMAP restriction is plausible given the stringent reduction of some staple cereals and legumes. However, in the long term we observed a greater proportion of patients meeting the dietary fibre nutrient requirements on an 'adapted FODMAP' diet having reintroduced foods high in FODMAPs to individual tolerance than for those patients who had returned to a 'habitual' diet. This may be due to increased familiarity with the diet and greater understanding of low-FODMAP high-fibre food choices.

Previous research suggests that FODMAP restriction leads to lower calcium intakes in the short term[13]. In the current study, mean calcium intakes were adequate and there was no difference in the proportion of patients that achieved their calcium requirement on an 'adapted FODMAP' diet compared with a 'habitual' diet. This may be due to a significant increase in lactose-free milk consumption (including calcium fortified plant-based milks) in the ''adapted FODMAP'' group such that calcium levels were maintained.

This is the first study to evaluate the intake of foods and food groups in patients following a low FODMAP diet. Patients who continued to follow an 'adapted FODMAP' diet had a lower intake of garlic, onion, ready-meals, some high fructan cereal-based foods (e.g. pasta), high FODMAP sugars (e.g. honey) and high FODMAP miscellaneous and processed foods compared with the 'habitual' diet. Cereal products including pasta, wheat bran and breakfast cereals have previously been identified as symptomatic triggers and the reduction of these is unsurprising[46]. A reduced intake of high fat foods and miscellaneous and processed high FODMAP foods for the 'adapted FODMAP' group signifies a move towards less high-fat, energy dense food options and may, in part, explain the reported weight loss observed in over 40% of those on an 'adapted FODMAP' diet. Previously, patients with IBS report greater induction of symptoms with fatty foods compared to controls[47] and those with IBS show hypersensitivity to lipid infusions compared to healthy individuals[48]. Interestingly, different proportions of fat, protein and carbohydrate may aggravate IBS, particularly IBS-C, via hormonal mediators of gut endocrine cells which are understood to regulate gastrointestinal functions including visceral sensation, motility and secretion[49]. In clinical practice, dietary manipulation of carbohydrate or fat or an increase in protein intake are associated with symptom improvements in some patients[49].

An increase of low FODMAP fruit and vegetables as seen here is equivalent to two portions of fruit and vegetables daily, again indicative of more healthful dietary patterns in the 'adapted FODMAP' group. Recent guidelines for IBS report that in a heterogeneous IBS population, lower intakes of fruit

and vegetables and higher intakes of fast foods have been reported to be involved in symptom generation although the evidence is insufficient to indicate that dietary habits have a role to play[22]. Thus, if a low FODMAP diet can improve dietary habits and decrease overall intake of foods high in fat in the long term; it may have additional benefits to health and warrants further research.

Further investigation to determine which individual FODMAPs and high FODMAP foods can be successfully reintroduced is of great interest and may help to determine whether any specific FODMAPs or foods are more likely to be tolerated, and which FODMAPs might be associated with provocation of specific symptoms.

A reduction in body weight has been observed in individuals randomised to a low FODMAP compared with 'habitual' diet[13] and a reduction in energy intake in another study[9]. Despite energy intake not being measured at baseline in the current study, 42% of patients reported weight reduction at long-term follow-up, this may be due to adopting a healthier eating pattern as described above. Weight and weight loss was self-reported and should be interpreted with caution[50].

To the best of our knowledge, this is the first study to investigate the long-term acceptability of the low FODMAP diet. We report the diet causes disruption for eating out and with family/friends. Consistent with a recent retrospective study, the diet was associated with increased cost[23]. All of these issues can be addressed during dietetic consultation[14, 15]. The low FODMAP diet does not negatively affect food-related QOL nor does it adversely affect enjoyment of meals, cooking, shopping and integration into current lifestyles compared with patients who consume their 'habitual' diet. Given the large proportion of individuals affected by IBS and the known reduction in their QOL[4] alongside dissatisfaction with current treatments by at least 60% of patients[51], these findings are of importance. They demonstrate that the diet is not only an effective treatment but it is acceptable with improved QOL for this chronic disorder and patients with inflammatory bowel disease[17, 23, 52].

The economic impact of IBS is notable[1, 53, 54]. Recent data suggest that IBS accounts for in excess of £80million in prescription costs alone and IBS patients are significant users of healthcare accounting for 7.5% of total outpatient visits across specialities[7]. The current findings indicate that healthcare usage and medication use is similar among those on an 'adapted FODMAP' diet and a 'habitual' diet, however the expenditure appears to be slightly lower than that reported for UK patients with IBS[1]. Further work is required to assess healthcare usage of patients who do and do not receive low FODMAP education.

There are several limitations of this study. Firstly, only 27% of the original sample invited to take part completed the study which is lower than other similar postal questionnaire studies[18, 57].Whilst we acknowledge that it is possible we may have sampled a biased population of patients who had responded to the low FODMAP diet, global symptom data from the baseline and short-term follow-up was similar for those who did and did not reply to the initial invite as reported previously[18]. Over 80% of subjects were recruited from an urban setting although most did not reply or had moved. Half of subjects invited from a rural area were recruited to the study. The higher response rate among these participants may possibly reflect the less transient nature of rural communities. In addition, the rural population were significantly older and included a smaller proportion of males than the urban population perhaps due to greater work opportunities for the younger population and for males in the urban area compared to elsewhere as reported from national data[58]. Secondly, the study design was a prospective questionnaire-based study that was uncontrolled and unblinded, thus increasing the risk of bias. Finally, given the lack of a disease activity biomarker in IBS, symptom evaluation was subjective and we acknowledge the limitations associated with subjective measures[22, 55]. Dietary intake was assessed by a food frequency questionnaire which has been validated to assess FODMAP intake however, not in a UK population. As with all food frequency questionnaires this approach can underestimate or overestimate intake of certain foods[56].

In summary, we report that the low FODMAP diet is an effective long-term strategy for the management of IBS addressing an area which has, to date, been largely unexplored[59-61].

Conclusion

This study prospectively evaluated the long-term impact of the low FODMAP diet on symptom response, dietary intake, patient acceptability and healthcare utilization in a large cohort of patients with IBS. Patients report that the diet is clinically effective with 57% reporting long-term satisfactory symptom relief. Individuals who have received comprehensive education on the low FODMAP diet have completed short-term FODMAP restriction followed by FODMAP reintroduction to individual tolerance. A low FODMAP diet can be nutritionally adequate up to 18 months after initial education and patients find that the diet is acceptable and does not adversely impact on food-related QOL.

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Disclosures

KW and MCL are cofounders of the FoodMaestro FODMAP app.

Table 1: Demographics of irritable bowel syndrome patients at long-term follow-up

Demographic	Long-term follow-up (n=103)	Secondary care (n=74)	Primary care (n=29)	P
Gender				
Female n (%)	76 (74)	50 (49)	26 (25)	0.022[2]
Male n (%)	27 (26)	24 (23)	3 (3)	
Age (years) mean ± SD	49 ± 15	45.3 ± 15	56.6 ± 12	<0.001[3]
Weight (kg) mean ± SD	69.7 ± 13.7	70.5 ± 13.7	68.0 ± 13.9	0.410[3]
BMI (kg/m^2) mean ± SD	24.8 ± 3.9	24.5 ± 3.6	25.2 ± 4.3	0.404[3]
Weight change since low FODMAP education				
Lost weight n (%)	42 (41)	31 (30)	11 (11)	0.064[2]
Remained the same weight n (%)	48 (47)	30 (29)	18 (18)	
Gained weight n (%)	13 (12)	13 (12)	0	
Knowledge and understanding of the low FODMAP diet n (%)[1]				
Average n (%)	35 (35)	28 (27)	7 (7)	0.465[2]
Above average n (%)	55 (56)	38 (37)	17 (17)	
Excellent n (%)	9 (9)	5 (5)	4 (4)	

[1] Missing n=4 [2] Chi squared between settings [3] Independent t-test between settings

Table 2: Intakes of energy, nutrients and FODMAPs for IBS patients at long-term follow-up

	Intakes (mean ± SD)					**Meeting requirements (DRV), n (%)**		
	Habitual diet (n=19)	**Adapted FODMAP diet (n=84)**	**P[1]**	**Dietary Reference Value[2]**		**Habitual diet n (%)**	**Adapted FODMAP diet n (%)**	**P[3]**
Energy kcal/d	2219 ± 831	2147 ± 759	0.715	2605 (m)	2079 (f)	11 (58)	43 (51)	0.597
Protein g/d	91.5 ± 38.0	99.1 ± 38.3	0.437	M 55.5	F 45	15 (79)	82 (98)	0.010
Fat g/d	87.7 ± 45.7	70.1 ± 33.4	0.056	35% of food energy		10 (53)	26 (31)	0.073
Carbohydrate g/d	250 ± 94.4	252 ± 95.5	0.925	50% of food energy		12 (63)	53 (63)	0.996
Starch g/d	122 ± 57.3	128 ± 56.9	0.696					
Total sugars g/d[4]	122 ± 55.2	122 ± 62.9	0.990					
Dietary fibre g/d	24.9 ± 9.47	26.8 ± 11.5	0.500	30		14 (74)	71 (85)	0.261
Calcium mg/d	960 ± 608	1168 ± 695	0.230	700		12 (63)	64 (76)	0.243
Iron mg/d	12.9 ± 4.10	13.9 ± 4.70	0.411	8.7 (m)	14.8 (f)	12 (63)	57 (68)	0.694
Zinc mg/d	12.7 ± 5.40	14.4 ± 5.35	0.231	M 9.5	F 7.0	15 (79)	79 (94)	0.058
Magnesium mg/d	342 ± 111	385 ± 134	0.198	M 300	F 270	14 (74)	64 (76)	0.243
Sodium g/d	2.70 ± 1.40	2.50 ± 1.40	0.849	1.6		14 (74)	60 (71)	0.843
Potassium g/d	3.77 ± 1.20	4.30 ± 1.50	0.191	3.5		11 (58)	54 (64)	0.602
Phosphorus mg/d	1757 ± 756	1879 ± 1340	0.704	550		19 (100)	83 (99)	0.816
Vitamin A ug/d[5]	1429 ± 845	2147 ± 1482	0.045	M 700	F 600	18 (95)	77 (92)	0.652
Thiamin mg/d	1.40 ± 0.60	1.87 ± 1.00	0.121	M 1.0	F 0.8	18 (95)	83 (99)	0.245
Riboflavin mg/d	2.37 ± 1.10	2.97 ± 1.60	0.093	M 1.3	F 1.1	16 (84)	83 (99)	0.019
Niacin mg/d	21.4 ± 7.00	25.37 ± 10.2	0.119	M 17	F 13	19 (100)	84 (100)	1.000
Folate ug/d	318 ± 108	398 ± 143	0.024	200		17 (90)	83 (99)	0.087
Vitamin C mg/d	168 ± 86.2	220 ± 143	0.129	40		19 (100)	84 (100)	1.000
Total FODMAPS g/d	29.4 ± 22.9	20.6 ± 14.9	0.039					
Fructo-oligosaccharides g/d	2.50 ± 1.30	2.00 ± 1.40	0.160					
Galacto-oligosaccharides g/d	1.00 ± 0.60	1.30 ± 1.50	0.326					
Lactose g/d	16.9 ± 19.4	10.4 ± 12.7	0.072					
Excess fructose g/d	6.20 ± 8.10	4.70 ± 10.4	0.561					
Sorbitol g/d	2.17 ± 1.90	1.60 ± 1.70	0.208					
Mannitol g/d	0.60 ± 0.60	0.50 ± 0.40	0.267					

DRV dietary reference value;

[1] Independent t-test between 'habitual' diet versus 'adapted FODMAP' diet

[2]Where applicable M male 19-50 years and F female 19-50 years values are given as an example but the value may not apply if >50 years [(30)]

[3] Chi squared between numbers meting the requirement (DRV) for 'habitual' diet versus 'adapted FODMAP' diet

[4] included sucrose, lactose, glucose and fructose – DRV only available for free sugars so not assessed

[5]Total vitamin A equivalents

Table 3: Dietary intake of high and low FODMAP food groups for IBS patients at long-term follow-up

Food group	Habitual diet (n=19) Mean ± SD (g/d)	Adapted FODMAP diet (n=84) Mean ± SD (g/d)	P
Cereals and grains high FODMAP	258 ±174	194 ± 146	0.098
Cereals and grains low FODMAP[1]	249 ±239	326 ± 247	0.221
Grain high FODMAP	21.8 ±27.1	15.79 ± 32.4	0.452
Grain low FODMAP	164 ±213	173 ± 177	0.859
Bread high FODMAP	76.6 ±75.0	61.4 ± 71.5	0.409
Bread low FODMAP[1]	1.56 ±5.31	28.6 ± 50.5	0.022
Breakfast cereal high FODMAP	47.4 ±46.8	43.4 ± 60.4	0.787
Breakfast cereal low FODMAP	23.2 ±34.8	28.6 ± 41.5	0.599
Pasta high FODMAP	47.5 ±55.7	20.8 ± 35.4	0.010
Pasta low FODMAP[1]	39.8 ±55.4	63.7 ± 77.3	0.204
Cereal products high FODMAP	29.5 ±27.4	22.7 ± 30.9	0.380
Cereal products low FODMAP[1]	20.4 ±25.7	32.5 ± 49.7	0.306
Milk & milk products high FODMAP	688 ±820	416 ± 529	0.074
Milk & milk products low FODMAP[2]	148 ±234	563 ± 777	0.023
Milk high FODMAP	552 ±830	295 ± 486	0.076
Milk low FODMAP[2]	82.7 ±157	476 ± 742	0.024
Cheese high FODMAP	7.31 ±18.3	11.8 ± 36.0	0.600
Cheese low FODMAP	27.5 ±38.2	29.3 ± 50.2	0.883
Yoghurt high FODMAP	97.5 ±141	94.5 ± 137	0.933
Yoghurt low FODMAP[2]	25.5 ±91.8	46.2 ± 103	0.422
Other dairy high FODMAP e.g. Ice cream	17.1 ±34.8	10.1 ± 18.2	0.211
Other dairy low FODMAP	7.38 ±11.6	5.91 ± 10.1	0.579
Fruit high FODMAP	233 ±176	188 ± 226	0.412
Fruit low FODMAP	289 ±227	460 ± 387	0.067
Vegetables high FODMAP	196 ±122	165 ± 170	0.453
Vegetables low FODMAP	488 ±250	708 ± 387	0.020
Proteins	184 ±126	199 ± 111	0.601
Fats	26.6 ±23.5	15.2 ± 12.5	0.003
Drinks high FODMAP	219 ±472	146 ± 350	0.441
Drinks low FODMAP	394 ±697	432 ± 536	0.791
Sugars high FODMAP[3]	11.7 ±17.6	4.15 ± 6.55	0.002
Sugars low FODMAP	15.4 ±16.8	20.5 ± 21.8	0.344
Miscellaneous and processed high FODMAP	194 ±152	117 ± 110	0.012
Miscellaneous and processed low FODMAP	70.2 ±104	53.8 ± 41.6	0.266
TOTAL high FODMAP	1751 ± 1015	1195 ± 658	0.004
TOTAL low FODMAP	1857 ± 983	2770 ± 1236	0.003

Independent t-test

[1] Foods described as gluten-free in the food frequency questionnaire were included in this group or sub-group

[2] Foods described as lactose-free in the food frequency questionnaire were included in this group or sub-group

[3] Includes honey, sugar-free chewing gum (high in polyols)

Table 4: The percentage of IBS patients consuming high FODMAP foods at least once a week at long-term follow-up

	Consumed at least once a week (% of patients)		
	Habitual diet	**Adapted FODMAP diet**	**P**
Fructans	30.2	21.1	<0.001
Galacto-oligosaccharides	28.8	24.5	0.11
Lactose	22.6	19	0.183
Free fructose	26.8	17	<0.001
Sorbitol	30.4	27	0.201
Mannitol	37.5	39.9	0.588

Table 5: Dietary acceptability and food-related quality of life of IBS patients at long-term follow-up

	Habitual diet n (%)			Adapted FODMAP diet n (%)			P
	Agree	**Neutral**	**Disagree**	**Agree**	**Neutral**	**Disagree**	
Dietary acceptability							
I find it easy to buy suitable foods for my current diet at my normal supermarkets or shops	14 (74)	1 (5)	4 (21)	57 (68)	9 (11)	18 (21)	0.759
I am able to buy foods suitable for my current diet at my normal supermarkets or shops[1]	16 (85)	1 (5)	2 (10)	63 (76)	9 (11)	11 (13)	0.698
I use high street/online speciality shops (e.g. health food shops) to buy food for my current diet	7 (41)	6 (35)	4 (24)	28 (33)	14 (17)	42 (50)	0.086
It takes extra time to shop for my current diet	8 (43)	5 (26)	6 (32)	54 (64)	11 (13)	19 (23)	0.172
It takes extra time to cook for my current diet	8 (42)	3 (16)	8 (43)	38 (45)	11 (13)	35 (42)	0.943
I find food labelling is adequate to allow me to confidently choose suitable foods	10 (53)	8 (42)	1 (5)	53 (63)	16 (19)	15 (17)	0.067
The cost of my current diet is more expensive	8 (42)	9 (47)	2 (11)	72 (86)	11 (13)	1 (1)	<0.001
Does eating out at restaurants make it more difficult for you to follow your current diet?	11 (58)	1 (5)	7 (37)	66 (79)	8 (10)	10 (12)	0.030
Does eating out at friends/families make it more difficult for you to follow your current diet?	9 (48)	3 (16)	7 (37)	61 (72)	15 (18)	8 (9)	0.009
Does travel (overseas/UK) make it more difficult for you to follow your current diet? [1]	9 (48)	3 (16)	7 (37)	63 (76)	11 (13)	9 (11)	0.014
Overall, I find my current diet tasty and enjoyable	14 (74)	3 (16)	2 (10)	53 (63)	15 (18)	16 (19)	0.622
I can incorporate my current diet easily into my life[1]	10 (55)	4 (22)	4 (22)	47 (56)	20 (24)	17 (20)	0.978
My current dietary needs have created stress with my family/friends[1]	5 (28)	3 (17)	10 (55)	20 (24)	16 (19)	48 (57)	0.929
Food-related quality of life							
Food and meals are positive elements of my life	14 (74)	3 (16)	2 (11)	57 (68)	14 (17)	13 (15)	0.842
I am generally pleased with my food	10 (53)	7 (37)	2 (11)	47 (56)	23 (27)	14 (16)	0.643
My life in relation to food and meals is close to my ideal[1]	9 (45)	5 (25)	6 (30)	25 (29)	27 (32)	32 (38)	0.329
With regard to food, the conditions of my life are excellent	8 (42)	7 (37)	4 (21)	27 (33)	28 (34)	28 (34)	0.535
Food and meals give me satisfaction in daily life	10 (53)	7 (37)	2 (10)	47 (56)	20 (24)	17 (20)	0.401
I wish my meals were much more pleasant part of my life[1]	6 (34)	6 (33)	6 (34)	35 (42)	20 (24)	29 (35)	0.674
When I think of my next meal, I only see problems, obstacles and disappointments[1]	4 (23)	5 (28)	9 (50)	15 (18)	17 (20)	52 (62)	0.189

[1] Missing n=1

Figure legends

Figure 1: Study flow diagram

Figure 2: Symptom relief for the global symptom question at each time-point

Figure 3: Proportion of patients reporting the presence of individual gastrointestinal symptoms at baseline, short-term follow-up and long term follow-up (n=103)

Baseline Short-term follow-up Long-term follow-up

P Significant differences between baseline and long-term follow-up

Figure 1

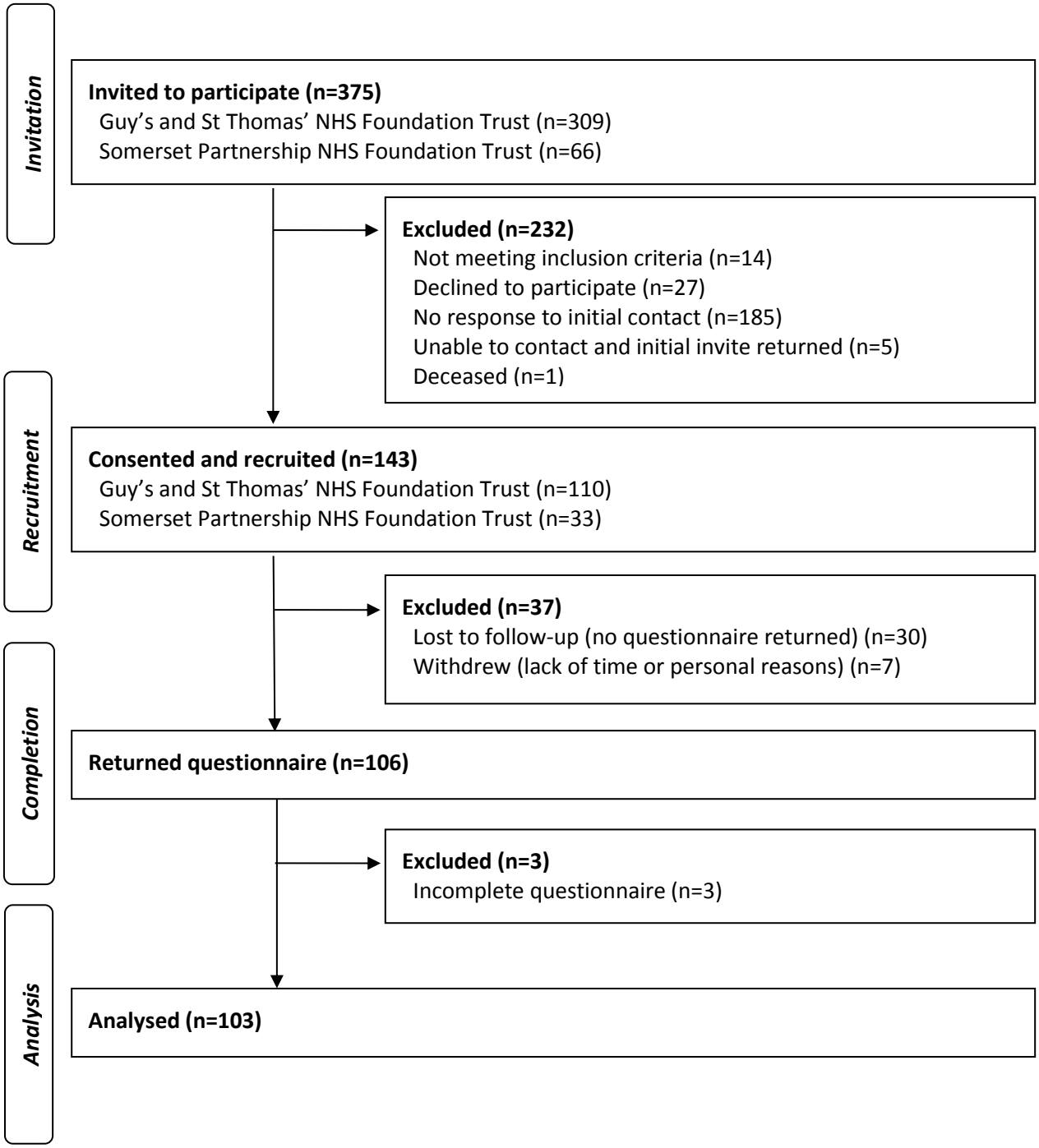

Invitation
Invited to participate (n=375)
Guy's and St Thomas' NHS Foundation Trust (n=309)
Somerset Partnership NHS Foundation Trust (n=66)
Excluded (n=232)
Not meeting inclusion criteria (n=14)
Declined to participate (n=27)
No response to initial contact (n=185)
Unable to contact and initial invite returned (n=5)
Deceased (n=1)
Recruitment
Consented and recruited (n=143)
Guy's and St Thomas' NHS Foundation Trust (n=110)
Somerset Partnership NHS Foundation Trust (n=33)
Excluded (n=37)
Lost to follow-up (no questionnaire returned) (n=30)
Withdrew (lack of time or personal reasons) (n=7)
Completion
Returned questionnaire (n=106)
Excluded (n=3)
Incomplete questionnaire (n=3)
Analysis
Analysed (n=103)

Figure 2

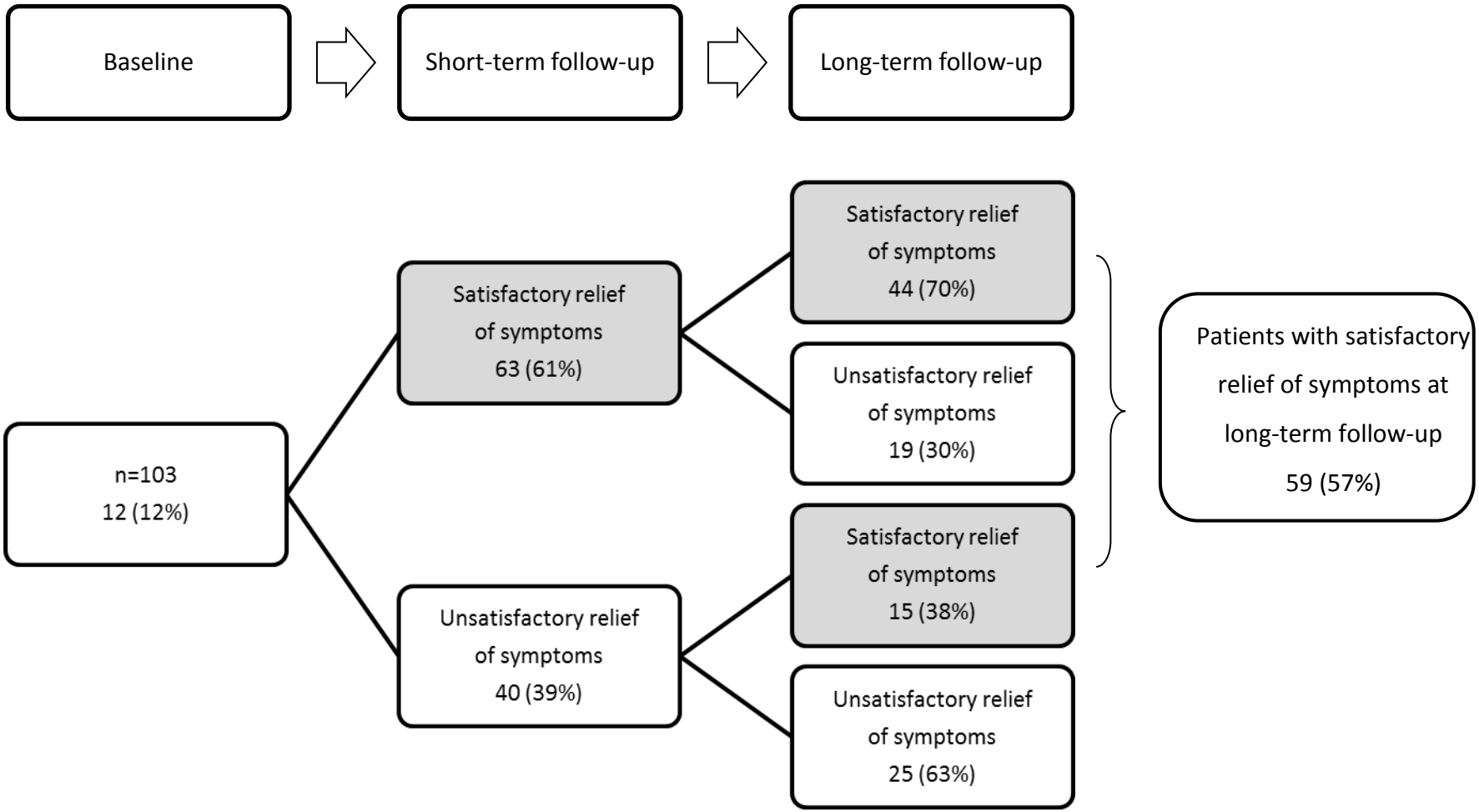
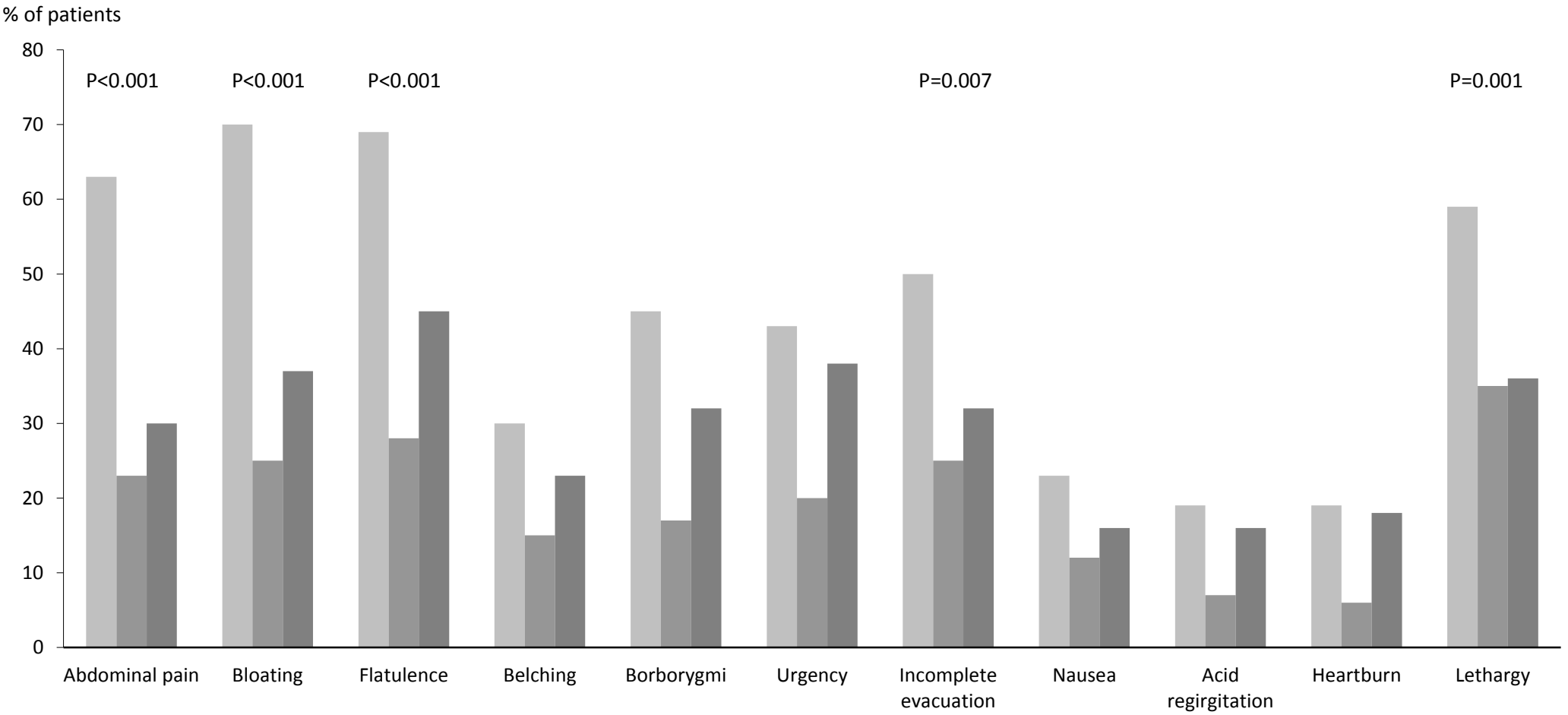

Baseline
Short-term follow-up
Long-term follow-up
n=103
12 (12%)
Satisfactory relief of symptoms 63 (61%)
Unsatisfactory relief of symptoms 40 (39%)
Satisfactory relief of symptoms 44 (70%)
Unsatisfactory relief of symptoms 19 (30%)
Satisfactory relief of symptoms 15 (38%)
Unsatisfactory relief of symptoms 25 (63%)
Patients with satisfactory relief of symptoms at long-term follow-up 59 (57%)

Figure 3


% of patients
80
70
60
50
40
30
20
10
0
P<0.001
P<0.001
P<0.001
P=0.007
P=0.001
Abdominal pain
Bloating
Flatulence
Belching
Borborygmi
Urgency
Incomplete evacuation
Nausea
Acid regirgitation
Heartburn
Lethargy

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